

changed claims as they should appear after entry of the amendment follows on the next page, and a version showing changes made to the changed claims is included at the end of this communication.



CLEAN VERSION OF CHANGED CLAIMS

D1
C1
1. (Twice Amended) A method for making a particulate product containing insulin, the method comprising:

contacting a feed solution containing insulin with a compressed anti-solvent fluid to precipitate particles containing insulin, the feed solution including the insulin in a cosolvent system, the cosolvent system comprising a first organic solvent and a second organic solvent that are mutually soluble, the first organic solvent and the second organic solvent not being the same; and

separating the particles from the anti-solvent fluid.

C2
2. (Amended) The method of claim 1, wherein insulin is at least an order of magnitude more soluble in the first organic solvent than in the second organic solvent.

D1
3. (Amended) The method of claim 1, wherein the first organic solvent and the second organic solvent are present in the solution at a volume ratio of the second organic solvent to the first organic solvent of larger than 30:70.

4. (Amended) The method of claim 1, wherein the first organic solvent and the second organic solvent are present in the cosolvent system at a volume ratio of the second organic solvent to the first organic solvent of from 50:50 to 90:10.

5. (Amended) The method of claim 1, wherein the concentration of insulin in the cosolvent system is smaller than 3 mg of insulin per milliliter of the feed solution.

6. (Amended) The method of claim 1, wherein the concentration of insulin in the cosolvent system is in a range of from 0.3 to 3 mg of insulin per milliliter of the solution.

7. (Amended) The method of claim 1, wherein the first organic solvent is selected from the group consisting of dimethyl sulfoxide and dimethyl formamide.

C3
D
10. (Amended) The method of claim 1, wherein the compressed anti-solvent, during the contacting, is at a reduced pressure of larger than 0.8 and a reduced temperature of larger than 0.95.

11. (Amended) The method of claim 10, wherein the compressed anti-solvent, during the contacting, is at a reduced pressure of larger than 0.9.

C4
D
15. (Amended) The method of claim 1, wherein, during the contacting step, the solution is introduced into the compressed anti-solvent fluid through an opening having a cross-

D1 sectional area available for flow that is larger than 1 square millimeter.

C4
conclude
16. (Amended) The method of claim 15, wherein the solution, when introduced into the compressed anti-solvent fluid has a direction of flow that is at an angle of from 45° to 180° relative to the direction of flow of the compressed anti-solvent fluid.

17. (Amended) The method of claim 1, wherein the cosolvent system includes water, if at all, in an amount of smaller than 5 weight percent.

C5 D1
19. (Amended) The method of claim 1, wherein the feed solution comprises colloidal particles of the insulin dispersed in the cosolvent system.

C6 D1
20. (Twice Amended) The method of claim 1, wherein the feed solution includes a biocompatible polymer and the particles are multi-component particles including the insulin and the biocompatible polymer.

C7 D1
24. (Amended) The method of claim 20, wherein the second organic solvent is selected from the group consisting of methylene chloride, formaldehyde, dioxolane, chloroform, benzene, ethyl ether, toluene, xylene, 1,3-dioxane and tetrahydrofuran.

C8 D1
27. (Amended) The method of claim 26, wherein the first organic solvent is selected from the group consisting of methanol, ethanol and isopropanol.

C9
D1
36. (Amended) The method of claim 30, wherein the weight ratio of the insulin to the polymer in the feed solution is larger than 5:95.

37. (Amended) The method of claim 20, wherein the weight ratio of the insulin to the polymer in the feed solution is in a range of from 5:95 to 50:50.

C10
39. (Amended) The method of claim 20, wherein the compressed anti-solvent fluid, during the contacting step, is at a reduced pressure of larger than 0.5 relative to the critical pressure of the anti-solvent fluid.

D1
40. (Amended) The method of claim 39, wherein the compressed anti-solvent fluid, during the contacting step, is at a reduced temperature of larger than 0.95 relative to the critical temperature of the anti-solvent fluid.

41. (Amended) The method of claim 40, wherein the compressed anti-solvent fluid, during the contacting step, is at a reduced pressure of larger than 0.8 relative to the critical pressure of the anti-solvent fluid.

C11
D1
45. (Amended) The method of claim 20, wherein during the contacting step, the feed solution is introduced into a flowing stream of the compressed anti-solvent fluid, the direction of

D
CM
each
flow of the feed solution, when introduced into the flowing stream of the compressed anti-solvent fluid, is at an angle of from 45° to 180° relative to the direction of flow of the compressed anti-solvent fluid.

D
C12
46. (Twice Amended) The method of claim 20, wherein the multi-component particles have a degree of encapsulation of the insulin by the polymer of greater than 50 percent.

47. (Twice Amended) The method of claim 20, wherein the multi-component particles have a degree of encapsulation of the insulin by the polymer of greater than 70 percent.
